

**REMARKS**

This Amendment filed in response to the non-final Office Action dated June 14, 2007, is believed to be fully responsive to the rejections raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

The presently claimed invention is now directed to a method for treating a stomach tumor comprising administering a composition containing benzyl alcohol and vitamin C. The Office Action of June 14, 2007 indicated that claims 1 - 3 and 16 - 17 were rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Said claims were also rejected under 35 U.S.C. § 103(a) as allegedly being obvious over the art of record. A telephonic Interview was conducted on September 13, 2007 to discuss the outstanding rejection and proposed amendments to overcome the rejection. In view of the discussion during the telephonic Interview, Applicant has amended the claims and submits that the rejections are rendered moot in view of the amendments set forth above.

In the present Amendment, claim 1 has been amended to improve its form and to recite that vitamin C is used in a range of 0.1 to 10 times 1 part of benzyl alcohol by weight. Support for the amendment can be found in the specification on page 8 at lines 3 to 6, for example.

No new matter has been added. Entry of the Amendment is respectfully submitted to be proper. Upon entry of the Amendment, claims 1-3, 16 and 17 will be all the claims pending in the application.

**I. Response to Claim Rejection - 35 U.S.C. § 112, Second Paragraph**

Claims 1-3 and 16-17 were rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite.

The Office Action alleged that the phrase “a dose of 1 mg-50 mg/tumor volume (cm<sup>3</sup>)” is unclear.

Applicant has amended claim 1 to improve its form. Claim 1, as amended, recites:

A method for treating a tumor comprising the step of administering a composition containing benzyl alcohol at a dose of 1 mg - 50 mg/cm<sup>3</sup> of tumor volume in combination with vitamin C, wherein vitamin C is used in a range of 0.1 to 10 times 1 part of benzyl alcohol by weight, wherein said dose is sufficient to cause cells of said tumor to become necrotic, and wherein said tumor is a stomach tumor.

In view of the amendment, Applicant respectfully requests withdrawal of the rejection.

The Office Action also indicated that the second recitation of “dose” in claim 1 is allegedly indefinite because it is unclear whether dose corresponds to 1 mg/cm<sup>3</sup> - 50 mg/cm<sup>3</sup> recited previously or whether there is another dose that corresponds to necrotic tumor cells.

Applicant traverses the rejection on the merits.

It is clear that “dose” corresponds to dose range of the active ingredient, benzyl alcohol. Support can be found in the specification on page 8 at lines 15 - 16.

Furthermore, during a telephonic Interview with Examiner James Anderson (who replaced the Examiner who had issued the Office Action) on September 13, 2007, Examiner Anderson stated that the claim language was not “unclear” as had been alleged by the previous

Examiner who had issued the Office Action. Withdrawal of the rejection is respectfully requested.

**II. Response to Claim Rejection Under 35 U.S.C. § 103(a)**

Claims 1-3 and 16-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,284,786 to Casciari et al. (hereinafter “Casciari et al.”) in view of “The anti-tumor effect to stomach cancer by benzyl alcohol,” Meeting of Japan Surgical Society on April 12-14, 2000, issued on March 2000, PP-1457 (hereafter “Reference PP-1457”) in light of Stedman’s Medical Dictionary, 25<sup>th</sup> Edition (1990), p. 1026-1027 (cited for definitions).

Applicant traverse the rejection on the merits.

Claim 1, the only independent claim, is drawn to a method for treating a tumor comprising the step of administering a composition containing benzyl alcohol at a dose of 1 mg - 50 mg/cm<sup>3</sup> of tumor volume in combination with vitamin C, wherein vitamin C is used in a range of 0.1 to 10 times 1 part of benzyl alcohol by weight, wherein said dose is sufficient to cause cells of said tumor to become necrotic, and wherein said tumor is a stomach tumor.

Claim 1 is patentable over Casciari et al and Reference PP-1457, *inter alia* because the references, alone or combined, do not teach or suggest each limitation of the claim. Neither Casciari et al. nor Reference PP-1456 teach or suggest the combination of ascorbic acid and benzyl alcohol. Nor is there any other reason for making the combination. Casciari et al. teaches a method of treating cancer using lipoic acid alone or in combination with ascorbic acid (vitamin C). (See col. 2, ll. 1-24, see also, claim 1). Casciari et al. also teaches that very high doses of ascorbic acid are preferentially toxic to tumors in the colon, pancreatic tumors and breast tumor

cells. Thus, Casciari et al. does not teach or suggest using vitamin C alone to treat stomach tumors.

Furthermore, Casciari et al. does not teach or suggest benzyl alcohol as a component of a composition used to treat cancer in the stomach.

Reference PP-1457 teaches that benzyl alcohol has anti-tumor effect in stomach cancer, but it does not teach or suggest a composition comprising both benzyl alcohol and vitamin C. Thus, the references, alone or combined do not teach or suggest the subject matter recited in claim 1. Nor is there any other reason to combine these references so as to arrive at the invention recited in claim 1.

Additionally, even if the references were combined, neither Casciari et al. nor Reference PP-1456 teaches or suggests a composition wherein the vitamin C is used in a range of 0.1 to 10 times 1 part of benzyl alcohol by weight.

Furthermore, Applicant respectfully requests reconsideration and withdrawal of the rejection in view of the certified experiment (result #2) provided in the Declaration Under 37 C.F.R. § 1.132 of Dr. Takeyama filed in the U.S. Patent and Trademark Office on April 14, 2006.

*Prima facie* obviousness can be rebutted by a showing of unexpected results. Applicant respectfully submits that the *in vitro* experiments based on the test results of Example 1 and Example 2 are predictive of the effectiveness of the composition *in vivo*.

In Example 1 of the specification, the tumor cells were implanted into a nude mouse and the increased volume of the tumor was calculated. Subsequently, the effective dose amount of benzyl alcohol, defined by the tumor volume, was determined.

Example 2 demonstrates that benzyl alcohol is effective at a dose of at least 1 mg - 50 mg/cm<sup>3</sup> tumor volume.

*In vitro* test data is sufficient and acceptable as being predictive of *in vivo* activity. Cross v. Iizuka, 753 F.2d 1040 (CAFC 1985). A copy of the case law is provided herewith for the Examiner's convenience.

The experiment in the § 1.132 Declaration was executed *in vitro* to obtain results for the combination of benzyl alcohol and vitamin C. The results show an effective combination of benzyl alcohol and vitamin C wherein the benzyl alcohol is effective at a dose of at least 1 mg - 50 mg/cm<sup>3</sup> tumor volume.

Lastly, Applicant submits that claim 1 has been amended to incorporate the limitation "the vitamin C is used in a range of 0.1 to 10 times per 1 part of benzyl alcohol by weight."

In view of the above, withdrawal of the rejection is respectfully requested.

### **III. Response to Arguments - 35 U.S.C. § 103**

A. The Office Action stated that Applicant's arguments of November 21, 2006 have been fully considered, but were not persuasive because the feature, "wherein vitamin C is used in a range of 0.1 to 10 times per 1 part of BA by weight," is supported in the specification and in the declaration, but is not recited in the claim.

Applicant submits that claim 1 has been amended to recite that vitamin C is used in a range of 0.1 to 10 times per 1 part of BA by weight. Withdrawal of the rejection is respectfully submitted to be proper.

B. Regarding the § 1.132 Declaration, the Office Action had indicated that the increase in cell death, reported on page 4 of the Declaration, is expected.

Applicant respectfully traverses for at least the reasons given above in Section II. In view of the amendment to claim 1, the arguments presented, and the explanation of the experiment and unexpected results provided in the 132 Declaration, withdrawal of the rejection is respectfully submitted to be proper.

#### IV. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The United States Patent & Trademark Office is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

AMENDMENT UNDER 37 C.F.R. § 1.111  
Application No.: 10/611,902

Attorney Docket No.: Q76104

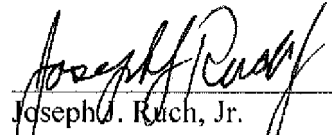
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**23373**

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1 of 1 DOCUMENT



Caution

As of: Oct 11, 2007

**PETER E. CROSS, ET AL., Appellants v. KINJI HIZUKA, ET AL., Appellees**

**No. 84-1111**

**UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT**

*753 F.2d 1040; 1985 U.S. App. LEXIS 14694; 224 U.S.P.Q. (BNA) 739*

**January 28, 1985**

**PRIOR HISTORY:**   [\*\*1]   Appealed from United States Patent & Trademark Office.

**LexisNexis(R) Headnotes**

**CASE SUMMARY:**

**PROCEDURAL POSTURE:** Appellant sought review of the decision of the United States Patent and Trademark Office Board of Patent Interferences awarding priority on a count to appellee in determination of applications filed by both parties under *35 U.S.C.S. § 119*.

**OVERVIEW:** Appellant and appellee submitted patent applications to the Board for priority of a pharmacological compound, each moving to be accorded a foreign priority application under *35 U.S.C.S. § 119* and asserting the other's application did not comply with the disclosure requirements of *35 U.S.C.S. § 112*. Because appellee filed the priority application first, appellee was declared the senior party and the Board held appellee's application contained an adequate how-to-use disclosure for the practical utility stated therein. Appellant sought review. The court held that where the Board was charged with the factual determination of utility and found the specifications of appellee's application disclosed the compound's utility and where credible evidence to support that factual determination existed, the determination would be upheld. As appellant bore the burden of proof to show that the Board erred in finding appellee's priority application adequately disclosed a practical utility and failed to do so, the Board's determination that appellee's application had a practical utility was upheld.

**OUTCOME:** The court affirmed the judgment.

***Patent Law > Utility Requirement > Proof of Utility***

[HN1] An invention cannot be considered useful, in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious.

***Patent Law > Utility Requirement > Proof of Utility***

[HN2] Where a constructive reduction to practice is involved, as contrasted to an actual reduction to practice, a practical utility for the invention is determined by reference to, and a factual analysis of, the disclosures of the application.

***Patent Law > Utility Requirement > Proof of Utility***

[HN3] Evidence of any utility is sufficient when the count does not recite any particular utility.

***Patent Law > Utility Requirement > Proof of Utility***

[HN4] A consideration in the determination of whether a patent should be granted is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point -- where specific benefit exists in currently available form -- there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.



**Patent Law > Jurisdiction & Review > Subject Matter  
Jurisdiction > Appeals**

**Patent Law > Utility Requirement > Chemical Com-  
pounds**

**Patent Law > Utility Requirement > Proof of Utility**

[HN5] Knowledge of the pharmacological activity of any compound is obviously beneficial to the public and adequate proof of any such utility constitutes a showing of practical utility.

**Patent Law > Utility Requirement > Proof of Utility**

[HN6] Where a count contains no limitation related to utility, evidence establishing a substantial utility for any purpose is sufficient to show a reduction to practice.

**Patent Law > Utility Requirement > Chemical Com-  
pounds**

[HN7] Every utility question arising in an interference, in the final analysis, must be decided on the basis of its own unique factual circumstances. Relevant evidence must be judged as a whole for its persuasiveness in determining whether the suggested use for the compound of the count is a practical utility.

**Patent Law > Utility Requirement > Chemical Com-  
pounds**

[HN8] A particular pharmacological activity identified with prior art compounds may have probative value as to the fact that the compound of the count possesses this particular pharmacological activity where there is a structural similarity between the prior art compounds and the compound of the count.

**Patent Law > Utility Requirement > Chemical Com-  
pounds**

**Patent Law > Utility Requirement > Proof of Utility**

[HN9] Adequate proof of any pharmacological activity constitutes a showing of practical utility.

**COUNSEL:** Rudolf E. Hutz, Connolly, Bove, Lodge & Hutz, of Wilmington, Delaware, argued for Appellants. With him on the brief was Thomas M. Meshbesh.

Peter D. Olexy, Sughrue, Mion, Zinn, MacPeak, & Seas, of Washington, District of Columbia, argued for Appellees. With him on the brief was Thomas J. MacPeak.

**JUDGES:** Kashiwa, Bennett, and Bissell, Circuit Judges.

**OPINION BY:** KASHIWA

**OPINION**

[\*1041] KASHIWA, Circuit Judge.

This appeal is from the decision of the United States Patent and Trademark Office (PTO) Board of Patent Interferences (Board) awarding priority on the single phantom count to Iizuka, *et al.* (Iizuka), the senior party. We affirm.

**Background**

Interference No. 100,650 was declared on 20 April 1981 between application serial No. 68,365, for "Imidazole Derivatives," filed by Iizuka on 21 August 1979 and application serial No. 95,755, for "N- (Phenoxyalkyl) Imidazoles as Selective Inhibitors of the Thromboxane Synthetase Enzyme and Pharmaceutical Compositions [\*1042] Thereof," filed by Cross, *et al.* (Cross) on 19 November 1979. The single phantom count of the interference is directed to imidazole [\*\*2] derivative compounds and reads as follows:

A compound selected from the group consisting of an imidazole derivative of the formula

[SEE ILLUSTRATION IN ORIGINAL]

wherein R is a hydrogen atom or an alkyl group having 1 to 6 carbon atoms, each of A[1] or A[2], which may be the same or different, are alkylene having 1 to 8 carbon atoms, m is 0 or 1, X is oxygen or sulfur, and each of R[1] or R[2], which may be the same or different, is a hydrogen atom or an alkyl group having 1 to 6 carbon atoms; R[3] is H, C[1]-C[4] alkyl, C[1]-C[4] alkoxy or halogen; and the pharmaceutically acceptable salts thereof.<sup>1</sup>

<sup>1</sup> We note a discrepancy, shown underlined in the above count, between the phantom count as set forth by the primary examiner and that reported by the Board in its decision. The phantom count set forth herein is the one propounded by the primary examiner. However, as will become apparent from the ensuing discussion, the substance of the phantom count is not crucial to resolution of the issues presented by this case.

[\*\*3] The applications of Cross and Iizuka both disclose inventions directed to imidazole derivative compounds which inhibit the synthesis of thromboxane synthetase, an enzyme which leads to the formation of

thromboxane A[2] (TXA[2]),<sup>2</sup> a highly unstable, biologically active compound which is converted to stable thromboxane B[2] by the addition of water. Thromboxane A[2], as of the time period during which the applications were filed, was postulated to be a causal factor in platelet aggregation.<sup>3</sup> Platelet aggregation is associated with several deleterious conditions in mammalia, including humans, such as platelet thrombosis, pulmonary vasoconstriction or vasospasm, inflammation, hypertension, and collagen-induced thrombosis.

2 The formation of TXA[2] in an arachidonic acid challenge is a sequential process initiated by the conversion of arachidonic acid to prostaglandin PGG[2] by the action of cyclooxygenase, which adds oxygen to the acid. Peroxidase converts the prostaglandin PGG[2] to prostaglandin PGH[2], which in turn is converted by thromboxane synthetase to TXA[2].

[\*\*4]

3 Iizuka's position is that, as of the "critical date" of his application, TXA[2] was widely accepted in the art as causing platelet aggregation. Cross' position is that, as of the "critical date," platelet aggregation was believed to be nonspecific, i.e., platelet aggregation *may* occur in the presence of thromboxane synthetase, but thromboxane synthetase is not necessary for platelet aggregation. We note in retrospect that THE MERCK INDEX 1345-46 (10th ed. 1983) describes TXA[2] as inducing irreversible platelet aggregation. More to the point, however, this court has noted that it is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests, nor is the inventor's theory or belief as to how his invention works a necessary element in the specification to satisfy the enablement requirement of 35 U.S.C. § 112. *Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1570, 219 U.S.P.Q. (BNA) 1137, 1140 (Fed. Cir. 1983).

Pursuant to 37 C.F.R. § 1.231(a)(4) each party moved to be accorded the benefit of the [\*\*5] foreign priority application under 35 U.S.C. § 119, Cross claiming priority based upon a British application filed 13 December 1978, and Iizuka claiming priority based upon a Japanese application filed 21 August 1978. Each party opposed the motion of the other party, each party contending that the other party's foreign priority application did not comply with the disclosure requirements of 35 U.S.C. § 112.

The primary examiner granted each party's motion, noting that the utility alleged in each application was of a pharmacological nature, i.e., the inhibition of thromboxane synthetase, and that inasmuch as the single phantom

count of the interference was directed to a compound, it was not necessary that utility be established by tests and dosages with respect to human beings. The examiner found that one of ordinary skill in the art would know how to use the imidazole derivatives, i.e., be able to determine specific dosages, for biological purposes. Based upon the filing dates of [\*1043] the foreign priority applications,<sup>4</sup> Iizuka was declared the senior party and a show cause order was issued against Cross.

4 Each party relies on the filing date of its foreign priority application to establish a constructive reduction to practice, the earliest date of invention to which each party is entitled under the patent laws of the United States. *Kawai v. Metlesics*, 480 F.2d 880, 885-86, 178 U.S.P.Q. (BNA) 158, 162 (CCPA 1973).

[\*\*6] Cross requested a final hearing on the issue of the sufficiency of the Japanese priority application of Iizuka, and moved for a testimony period to present evidence on this issue. A testimony period was granted over the opposition of Iizuka, and Cross took the testimony of his expert witness, Dr. Smith, and Iizuka took the testimony of his expert witness, Dr. Ramwell and also proffered several exhibits pursuant to 37 C.F.R. § 1.282. All testimony and exhibits related to the sufficiency of Iizuka's Japanese priority application, i.e., whether it complied with the disclosure requirements of 35 U.S.C. § 112.

#### *Decision of the Board*

The Board noted that the sole issue before it was whether Iizuka was entitled to the benefit of his Japanese priority application.<sup>5</sup> Relying on *In re Bundy*, 642 F.2d 430, 209 U.S.P.Q. (BNA) 48 (CCPA 1981), and *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (CCPA 1980), the Board held that tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use. The Board found that the Japanese priority application disclosed pharmacological activity in the similar [\*\*7] activity of the imidazole derivatives of the count to imidazole and 1-methylimidazole, which possess an inhibitory action for thromboxane synthetase, and that practical utility was disclosed in the strong inhibitory action for thromboxane synthetase from human or bovine platelet microsomes, i.e., an *in vitro* utility.<sup>6</sup>

5 More specifically, the issue before the Board was whether the Japanese priority application complied with the how-to-use requirement of 35 U.S.C. § 112. Section 112 of Title 35 provides, in pertinent part, that:

The specification shall contain a written description of the invention,

of the manner and process of making and *using* it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and *use* the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention. (Emphasis added.)

Should Iizuka's Japanese priority application be found nonenabling with respect to the how-to-use requirement of § 112, or otherwise found deficient under the patent laws of the United States, priority would be awarded to Cross based upon his unchallenged entitlement to the benefit of his British application.

[\*\*8]

6 Generally, *in vitro* refers to an environment outside of a living organism, usually an artificial environment such as a test tube or culture. In contradistinction, *in vivo* generally refers to an environment within a living organism, such as a plant or animal, or it may refer to a particular portion of an organ external to the living organism, e.g., rat aortic loop.

The Board further found that the Japanese priority application disclosed "how-to-use" knowledge directed to the practical utility in a microsome system, and that microsome assays were admittedly known in the art. A skilled worker could determine the relative strength of the imidazole compounds of the count vis-a-vis the known parent imidazole and 1-methylimidazole compounds for use in the microsome assay milieu. Knowledge of the pharmacological activities of compounds is beneficial to the medical profession, and requiring Iizuka to have disclosed *in vivo* dosages in the Japanese priority application would delay and frustrate researchers by failing to provide an incentive for early public disclosure of such compounds, [\*\*9] thereby failing to further the public interest.

Accordingly, the Board held that the Japanese priority application contained an adequate how-to-use disclosure for the practical utility stated therein.

#### Issues

Whether the Board erred in finding that the utility disclosed in the Japanese priority application is sufficient to meet the practical utility requirement of 35 U.S.C. § 101.

[\*1044] Whether the Board erred in finding that the Japanese priority application contained sufficient disclosure to satisfy the enablement, i.e., how-to-use, requirement of 35 U.S.C. § 112.<sup>7</sup>

7 Utility is a fact question. *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 956, 220 U.S.P.Q. (BNA) 592, 596 (Fed. Cir. 1983), cert. denied, 469 U.S. 835, 105 S. Ct. 127, 83 L. Ed. 2d 69, 225 U.S.P.Q. (BNA) 232 (1984). Enablement under § 112, paragraph 1, i.e., the how-to-use requirement, is a question of law. *Id.* at 960 n.6, 220 U.S.P.Q. (BNA) at 599 n.6.

#### OPINION

Proper resolution of the issues before this [\*\*10] court necessitates that we address, *seriatim*, the following questions: (1) What utility is disclosed by the Japanese priority application? (2) Does this stated utility comply with the "practical utility" requirement of 35 U.S.C. § 101, as delimited by prior decisions of the judiciary? \* (3) Does the Japanese priority application contain sufficient disclosure to meet the how-to-use requirement of § 112 with respect to the stated utility?

8 While questions one and two are closely connected, a thorough analysis of the utility issue requires first, a determination as to what utility is disclosed, i.e., the stated utility, for the invention claimed in the application. Only after the stated utility has been determined, can a proper analysis be undertaken to determine if the stated utility complies with the "practical utility" requirement of § 101. As noted above, these questions regarding utility are factual in nature, *see supra* note 7, and are to be determined in the first instance by the PTO, the agency with the expertise in this regard.

[\*\*11] It is axiomatic that [HN1] an invention cannot be considered "useful", in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious. *Brenner v. Manson*, 383 U.S. 519, 16 L. Ed. 2d 69, 86 S. Ct. 1033, 148 U.S.P.Q. (BNA) 689 (1966). [HN2] Where a constructive reduction to practice is involved, as contrasted to an actual reduction to practice, a practical utility for the invention is determined by reference to, and a factual analysis of, the disclosures of the application. *Kawai v. Mellesics*, 480 F.2d 880, 178 U.S.P.Q. (BNA) 158 (CCPA 1973).

#### 1. Japanese Priority Application

The Board factually analyzed the Japanese priority application and found that the only effective disclosure

relating to a stated utility for the imidazole derivative compounds of the phantom count was the following:

[The compounds disclosed] are useful for treatment of inflammation, thrombus, hypertension, cerebral apoplexy, asthma, etc.

Up to this time, it is a known fact that imidazole and 1-methylimidazole possess an inhibitory action for thromboxane synthetase and inhibit a biosynthesis [\*\*12] of thromboxane A[2]. (*Prostaglandins*, Vol. 13, pages 611-, 1977). However, since their inhibitory effect is not satisfactory one, these compounds have not been put to practical use yet as therapeutic medicines for diseases caused by thromboxane A[2], such as inflammation, hypertension, thrombus, cerebral apoplexy, asthma, etc.

To develop some compounds possessing a strong inhibitory action for biosynthesis of thromboxane A[2], the present inventors devoted themselves to study for various imidazole derivatives, and as a result, found that the compounds [of this invention] possess a strong inhibitory action for thromboxane synthetase from human or bovine platelet microsomes and are extremely useful as therapeutically active agents for diseases caused by thromboxane A[2], for example, inflammation, hypertension, thrombus, cerebral apoplexy, asthma, etc., and thus we proposed this invention based upon those findings.

\* \* \*

The imidazole derivatives . . . of this invention are novel compounds which are not described in literature, and which possess a strong inhibitory action for thromboxane synthetase from human or bovine platelet microsomes, and which [\*1045] [\*\*13] exhibit a strong inhibitory action for biosynthesis of thromboxane A[2] in mammalia including human. In general, a satisfactory inhibitory effect is found at a level of molar concentrations of  $2.5 \times 10^{-8}$ , for example, 2-[p-(1-imidazolyl)methyl]phenoxy-acetic acid hydrochloride produce the about 50% inhibitory effect at the molar concentrations of  $2.5 \times 10^{-8}$ . Accordingly, the imidazole derivatives of

this invention are extremely useful as therapeutic medicines for diseases caused by thromboxane A[2], such as inflammation, hypertension, thrombus, cerebral apoplexy, asthma, etc.

The Board found that these pertinent sections of the Japanese priority application disclosed some activity or utility, namely that the imidazole derivative compounds of the count possess a strong inhibitory action for thromboxane synthetase in human or bovine platelet microsomes. Cross' position is that the stated purpose or sole contemplated utility of the invention of Iizuka is to provide a novel class of compounds which provide "practical use" as "therapeutic medicines for diseases caused by thromboxane A[2]," and therefore the Board erred in its finding as to the stated utility [\*\*14] of the Japanese priority application.

While recognizing that *Kawai* constrains an applicant to entitlement to the benefit of only what is disclosed in the foreign priority application and no more, we also recognize that foreign priority applications, as subsequently filed in the PTO, typically have a style and format dissimilar to the arrangement of application elements suggested by 37 C.F.R. § 1.77. In part this arises because of differences in filing requirements in foreign patent offices, and in part because of the awkwardness resulting from direct literal translations from a foreign language to English. Thus, while the factual determination of the stated utility in an application prepared in the United States may be relatively straightforward,<sup>9</sup> the factual analysis of a foreign priority application to determine the utility disclosed therein may be more laborious and open to varying interpretations.

9 In applications prepared in the United States by experienced patent drafters, the drafter of the application typically sets forth objectives for the invention in the "Summary of the Invention" section of the application. These objectives will normally be consonant with the utility disclosed for the invention. As this court has noted, "when a properly claimed invention meets at least one stated objective, utility under § 101 is clearly shown." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. (BNA) 592, 598 (Fed. Cir. 1983), cert. denied, 469 U.S. 835, 105 S. Ct. 127, 83 L. Ed. 2d 69 (1984).

[\*\*15] The weakness of Cross' position is that a fair reading of the pertinent sections of the Japanese priority application, as set forth above, discloses utility for the imidazole derivative compounds of the phantom count both as an inhibiting agent for thromboxane synthetase in

human or bovine platelet microsomes, as found by the Board, and as therapeutically active agents preventing the biosynthesis of thromboxane A[2], thereby functioning as a medicine preventing deleterious conditions caused by thromboxane A[2], as contended by Cross.

[HN3] Evidence of any utility is sufficient when the count does not recite any particular utility. *Nelson v. Bowler*, 626 F.2d 853, 856, 206 U.S.P.Q. (BNA) 881, 883 (CCPA 1980). See also *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 181 U.S.P.Q. (BNA) 453 (CCPA 1974); *Knapp v. Anderson*, 477 F.2d 588, 177 U.S.P.Q. (BNA) 688 (CCPA 1973); *Blicke v. Treves*, 44 C.C.P.A. 753, 241 F.2d 718, 112 U.S.P.Q. (BNA) 472 (CCPA 1957). Here the Board, which is charged with the factual determination of utility,<sup>10</sup> has found that the specification of the Japanese priority application disclosed a utility for the imidazole derivative compounds of the phantom [\*16] count in the inhibition of thromboxane [\*1046] synthetase in human or bovine platelet microsomes. Inasmuch as the Board is charged with making this factual determination when the issue is raised, inasmuch as they have so done in the instant case, and inasmuch as there is credible evidence to support this factual determination, we are not prepared to say that the Board erred in its finding as to the stated utility disclosed in the Japanese priority application.

10 Under the facts of the instant case, utility and enablement questions are ancillary to priority. In the interference proceeding, Cross raised the issue as to whether the Japanese priority application contained sufficient disclosure to satisfy § 112. As noted above, see *supra* note 5, if Cross prevails on this issue the Japanese priority application would be removed as the basis for awarding priority to Iizuka. See generally 37 C.F.R. §§ 1.225, 231, 258.

## 2. Practical Utility

As noted in the preceding part of this opinion, Cross [\*17] has contended that the Board erred in its finding as to the utility disclosed in the Japanese priority application. This argument may be viewed in a different perspective, we believe, which is that the stated utility in the Japanese priority application, as found by the Board -- the inhibition of thromboxane synthetase in human or bovine platelet microsomes<sup>11</sup> -- is not sufficiently correlated to a pharmacological activity<sup>12</sup> to be a practical utility. In other words, Cross may be arguing that the minimum acceptable level of utility disclosed in an application claiming a compound having pharmacological activity must be directed to an *in vivo* utility in order to comply with the practical utility requirement of § 101.

11 A platelet microsome is an *in vitro* milieu consisting of blood platelets, the small, colorless corpuscles in the blood of all mammals, and other finely granular elements of protoplasm, such as ribosomes, fragmented endoplasmic reticula and mitochondrial cristae.

12 Generally, pharmacological activity refers to the properties and reactions of drugs, especially with relation to their therapeutic value.

[\*18] The starting point for a practical utility analysis is *Brenner v. Manson*, 383 U.S. 519, 16 L. Ed. 2d 69, 86 S. Ct. 1033, 148 U.S.P.Q. (BNA) 689 (1966). The Court in *Brenner* noted that "a simple, everyday word ["useful," as found in 35 U.S.C. § 101] can be pregnant with ambiguity when applied to the facts of life." *Id.* at 529, 148 U.S.P.Q. (BNA) at 693. [HN4] While noting that "one of the purposes of the patent system is to encourage dissemination of information concerning discoveries and inventions," *id.* at 533, 148 U.S.P.Q. (BNA) at 695, the Court found that a more compelling consideration in the determination of whether a patent should be granted "is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point -- where specific benefit exists in currently available form -- there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." *Id.* at 534-35, 148 U.S.P.Q. (BNA) at 695. While we recognize that this case concerned a compound derived from a chemical process, we believe *Brenner* provides broad guidelines which are helpful in [\*19] ascertaining what constitutes practical utility for compounds having a pharmacological effect.

[HN5] In *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (1980), our predecessor court, the Court of Customs and Patent Appeals, stated that "knowledge of the pharmacological activity of any compound is obviously beneficial to the public" and concluded that "adequate proof of any such utility constitutes a showing of practical utility." *Id.* at 856, 206 U.S.P.Q. (BNA) at 883.<sup>13</sup> The tests<sup>14</sup> found by the court to be adequate proof of pharmacological activity or practical utility were a rat blood pressure (BP) test and a gerbil colon smooth muscle stimulation (GC-SMS) test. The BP test was an *in vivo* test, which was deemed by the court to be direct evidence as to the claimed [\*1047] activity, while the GC-SMS test was an *in vitro* test.<sup>15</sup>

13 For purposes of the present opinion, we consider the phrase "substantial utility," as enunciated in *Brenner*, to be synonymous with the phrase "practical utility" as used in subsequent opinions of the CCPA.

14 We recognize that *Nelson* dealt with tests which were found adequate to establish an actual reduction to practice, as opposed to a constructive reduction to practice. We agree with the Board that principles applicable to a determination of an actual reduction to practice are generally germane to a constructive reduction to practice.

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15 Both parties admitted that the GC-SMS test adequately simulated *in vivo* smooth muscle stimulation.

The CCPA in *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. (BNA) 453, 454 (1974), stated that [HN6] where a count contains no limitation related to utility, evidence establishing a substantial utility for any purpose is sufficient to show a reduction to practice. The court held that three *in vivo* tests<sup>16</sup> conducted in the United States prior to the filing of Engelhardt's U.S. application failed to establish an actual reduction to practice. The court proceeded, however, to find sufficient evidence in the record to establish that Engelhardt had conceived a utility for his compound prior to the filing date of his U.S. application. The evidence the court found to be sufficient was testimony by the inventor that he believed his compound would exhibit a particular pharmacological activity because of its structural similarity to another compound which was known to possess the particular pharmacological activity. The court found that the testimonial evidence of Engelhardt [\*\*21] was corroborated by two exhibits entered into evidence. The evidence adduced by Engelhardt was found by the court to be sufficient proof that Engelhardt had conceived that his compound had utility for the particular pharmacological activity prior to his U.S. filing date. The court further noted that this was a completed conception of utility because it appeared that nothing beyond the exercise of routine skill would have been required to demonstrate that Engelhardt's compound possessed the particular pharmacological utility. While noting that the actual testing done was not sufficient to establish an actual reduction to practice, the court found that the extensive testing done *in vivo* on animals was routine in nature and was not, therefore, to be construed as an indicator that extensive research, i.e., inventive skill and/or undue experimentation, was required to resolve perplexing intricate difficulties related to the utilization of the compound for the particular pharmacological activity.

16 The three tests, all *in vivo* type tests carried out on laboratory animals, were: (1) the Mental Health General Screening Test which indicated the physical response, or absence of a response, of test animals to a drug, indicating the presence, or absence, of a desired pharmacological activity; (2) the Tetrabenazine Antagonism Test which screened drugs for antidepressant activity; and (3)

the Sidman Avoidance Test which screened drugs for tranquilizing activity.

[\*\*22] The CCPA in *Kawai v. Metlesics*, 480 F.2d 880, 178 U.S.P.Q. (BNA) 158 (1973), concurred with the finding of the Board that the applicants had failed to prove that their foreign priority application was adequate under the patent laws of the United States. The only disclosure in the foreign priority application relating to the compound of the count was that it exhibited "pharmacological effects on the central nervous system," which the applicants conceded was an inadequate disclosure. The applicants, however, relied upon a patent made of record as indicative of the general knowledge of one skilled in the art, which the applicants contended described a compound closely related to their claimed compound, to show utility or pharmacological activity for the compound of the count as an anticonvulsant. The court agreed with the board that there were sufficient structural dissimilarities between the compounds of the patent and those of the count to preclude reliance on the patent to supplement the disclosure deficiencies of the foreign priority application.

In *Knapp v. Anderson*, 477 F.2d 588, 177 U.S.P.Q. (BNA) 688 (CCPA 1973), the court, citing to *Blicke v. Treves*, 44 C.C.P.A. [\*\*23] 753, 241 F.2d 718, 112 U.S.P.Q. (BNA) 472 (CCPA 1957), stated that "it is well settled that if the counts do not specify any particular use, evidence proving *substantial utility for any purpose* is sufficient to establish an actual reduction to practice." *Id.* at 590, 177 U.S.P.Q. (BNA) at 690 (emphasis added). Noting that the only utility contemplated for the compounds of the count was as ashless dispersants in lubricant compositions used in internal combustion engines, the court found no error in the Board's holding that there was no actual reduction to practice because [\*1048] only a potential utility had been established, this holding based upon the Board's finding of a lack of correlation between bench tests and actual service conditions in a combustion engine.

The CCPA has held that nebulous expressions, such as "biological activity" or "biological properties," disclosed in a specification convey little explicit indication regarding the utility of a compound. *In re Kirk*, 54 C.C.P.A. 1119, 376 F.2d 936, 941, 153 U.S.P.Q. (BNA) 48, 52 (CCPA 1967). But, while agreeing with the Board that the specification failed to disclose a specific allegation of utility for [\*\*24] any compound within the scope of the claims, and that reference in the specification to biological properties of the claimed compound was so general and vague as to be meaningless, the court implied that a disclosure in the specification that the requisite properties of the claimed compounds are similar to those of a natural or synthetic hormone of known activity may, in appropriate circumstances, supplement an application to rectify an inadequate disclosure relating to the practical

utility for the compound. *Id.* at 942, 153 U.S.P.Q. (BNA) at 53.

[HN7] Every utility question arising in an interference, in the final analysis, must be decided on the basis of its own unique factual circumstances. Relevant evidence must be judged as a whole for its persuasiveness in determining whether the suggested use for the compound of the count is a practical utility. *Cf. Nelson*, 626 F.2d at 858, 206 U.S.P.Q. (BNA) at 885.

The Board has found that the Japanese priority application of Iizuka disclosed a practical utility for the compounds of the phantom count in the inhibition of thromboxane synthetase in human or bovine platelet microsomes, i.e., an *in vitro* utility. Clearly, this stated [\*\*25] utility as found by the Board has been delimited with sufficient specificity to satisfy the threshold requirements of *Kawai* and *Kirk*. The stated utility of the Japanese priority application is directed to a specific pharmacological activity possessed by the imidazole derivatives of the phantom count -- the inhibition of thromboxane synthetase *in vitro*. Thus, this court on review is not presented with a general allegation of "biological activity" or "biological properties" as was the CCPA in *Kirk*, nor is reliance on prior art required to ascertain what specific pharmacological activity the compound of the count possesses, the factual situation confronting the court in *Kawai*.

The Japanese priority application, moreover, disclosed that it was generally known in the art, as of the critical date, that the parent imidazole and 1-methylimidazole compounds possessed an inhibitory action for thromboxane synthetase. Reliance on this disclosure in the specification of the pharmacological property of the parent imidazole and 1-methylimidazole compounds, as going towards proof of the pharmacological activity of the imidazole derivatives of the phantom count, is particularly [\*\*26] relevant in the instant case, we believe, because Iizuka is not relying on this inference to supplement an inadequate disclosure in the Japanese priority application regarding the pharmacological activity of the compound of the phantom count, but rather is relying on this inference as cumulative probative evidence showing an adequately disclosed practical utility in the Japanese priority application.

This court, in *Rey-Bellet* and *Kawai*, has implied that [HN8] a particular pharmacological activity identified with prior art compounds may have probative value as to the fact that the compound of the count possesses this particular pharmacological activity where there is a structural similarity between the prior art compounds and the compound of the count. *Rey-Bellet*, 493 F.2d at 1385-87, 181 U.S.P.Q. (BNA) at 456-58; *Kawai*, 480 F.2d at 890-91, 178 U.S.P.Q. (BNA) at 166-67. Cross has failed

to proffer sufficient evidence or present any persuasive arguments going to the question of significant structural dissimilarities between the parent imidazole and 1-methylimidazole compounds and the imidazole derivatives of the phantom count. <sup>17</sup>

17 Contrary to Cross' contention in the Reply Brief, the evidence of record relied upon by Cross to show significant structural dissimilarity appears to us to be directed to the fact that there is a wide disparity in potency for thromboxane synthetase inhibition between the parent imidazole compound and prior art imidazole derivatives. Cross has not directed our attention to any specific evidence of record which establishes, or tends to establish, significant structural dissimilarities between the basic imidazole compound and the imidazole derivatives of the phantom count. Variation in potency, moreover, is a matter of degree of activity, *see Bundy*, 642 F.2d at 433, 209 U.S.P.Q. (BNA) at 51, but is still indicative of activity. There is no requirement that the compounds have the same degree of activity. *Id.*, 209 U.S.P.Q. (BNA) at 51. Moreover, this argument may be construed as a tacit admission that the parent imidazole compound does possess the particular pharmacological activity of inhibiting thromboxane synthetase.

Along this line, we note that Dr. Smith, Cross' expert witness, testified generally, based upon the exhibits proffered by Iizuka, *see infra* note 18, that the parent imidazole compound possessed pharmacological activity for inhibiting thromboxane synthetase, although stating that there was a wide potency spectrum for prior art imidazole derivatives with respect to the parent imidazole compound.

Cross has directed the court's attention to the fact that the Japanese priority application, while disclosing that the parent imidazole and 1-methylimidazole compounds possess an inhibitory action for thromboxane synthetase, further discloses that this inhibitory effect is not satisfactory and that the parent imidazole and 1-methylimidazole compounds have not been put to practical therapeutic use. But a therapeutical utility is not necessarily synonymous to a pharmacological activity. *Cf. Nelson*, 626 F.2d at 856, 206 U.S.P.Q. (BNA) at 883.

[\*\*27] [\*1049] The expert of Iizuka, Dr. Ramwell, testified that, as of the critical date, there was an awareness on the part of those skilled in the art that the parent imidazole compound exhibited an inhibitory activity for thromboxane synthetase, in both *in vitro* and *in vivo* en-

vironments. Dr. Ramwell further testified that there was an awareness by those skilled in the art of a correlation between thromboxane A[2] and platelet aggregation, namely that thromboxane A[2] was a mediator in platelet aggregation. Several exhibits proffered by Iizuka corroborated Dr. Ramwell's testimony as to the general knowledge in the art with respect to the inhibitory effect of the parent imidazole compound for thromboxane synthetase.<sup>18</sup> Accordingly, the similar pharmacological activity of the parent imidazole and 1-methylimidazole compounds have probative value in the factual determination of practical utility for the compounds of the phantom count inasmuch as Cross has not met the burden of proof to establish structural dissimilarities between the parent imidazole and 1-methylimidazole compounds and the imidazole derivatives of the phantom count. *Rey-Bellet*, 493 F.2d at 1386-87, [\*\*28] 181 U.S.P.Q. (BNA) at 457.

18 For example, Table I in the article "Imidazole: A Selective Inhibitor of Thromboxane Synthetase," PROSTAGLANDINS, Vol. 13, No. 4, April 1977 (Iizuka Exhibit No. 6), lists 1-methylimidazole and the parent imidazole compounds as possessing inhibitory activity for thromboxane synthetase, thereby offering corroboration of Dr. Ramwell's testimony.

The Board noted that Iizuka Exhibits 2-6 and 10-12, while inadmissible for the purpose of establishing the truth of what they say on their face, are admissible to bolster and support the testimony of Dr. Ramwell, as well as for the purpose of establishing what literature was available to the art at the critical time. Thus, for review purposes, we have examined these exhibits for their corroborating value with respect to Dr. Ramwell's testimony.

The Board found that there was adequate proof that the Japanese priority application disclosed a pharmacological activity for the compounds of the phantom count in inhibiting the action of [\*\*29] thromboxane synthetase, similar to the pharmacological activity of the parent imidazole and 1-methylimidazole compounds which were found to possess an inhibitory action for thromboxane synthetase, this disclosed knowledge of the inhibitory action of the prior art compounds having been corroborated by testimony and documentary evidence. During the proceedings before the Board, the burden of proof rested upon Cross to show that the Japanese priority application was deficient. 37 C.F.R. § 1.257(a). On review, Cross bears the burden of proof to show that the Board erred in finding that the Japanese priority application had adequately disclosed a practical utility. Reviewing the

relevant evidence presented to the Board as a whole, we are not persuaded that Cross has met this burden of proof.

[\*1050] The final question we must address is whether the inhibitory activity for thromboxane synthetase in human or bovine platelet microsomes, i.e., an *in vitro* utility, is sufficient to comply with the practical utility requirement of § 101. Based upon the facts of this case, we are not persuaded that the Board erred in finding that the *in vitro* utility disclosed in the Japanese [\*\*30] priority application for the compounds of the count is sufficient to establish a practical utility.

Our predecessor court has noted that [HN9] adequate proof of any pharmacological activity constitutes a showing of practical utility. See, e.g., *Nelson*, 626 F.2d at 856, 206 U.S.P.Q. (BNA) at 883; *Rey-Bellet*, 493 F.2d at 1383, 181 U.S.P.Q. (BNA) at 454. Dr. Ramwell testified that initial testing of compounds for a particular pharmacological activity is typically done *in vitro*. *In vitro* testing permits an investigator to establish the rank order of compounds with respect to the particular pharmacological activity, i.e., to determine the relative potency of the compounds. Compounds having the highest ranking or potency are then selected for further testing *in vivo*. Presumably this is the accepted practice in the pharmaceutical industry inasmuch as Cross has not proffered any evidence refuting this testimony of Dr. Ramwell, and we note that this practice has an inherent logical persuasiveness. *In vitro* testing, in general, is relatively less complex, less time consuming, and less expensive than *in vivo* testing. Moreover, *in vitro* results with respect to the particular [\*\*31] pharmacological activity are generally predictive of *in vivo* test results, i.e., there is a reasonable correlation therebetween. Were this not so, the testing procedures of the pharmaceutical industry would not be as they are. Iizuka has not urged, and rightly so, that there is an invariable exact correlation between *in vitro* test results and *in vivo* test results. Rather, Iizuka's position is that successful *in vitro* testing for a particular pharmacological activity establishes a significant probability that *in vivo* testing for this particular pharmacological activity will be successful.

As discussed above, Dr. Ramwell testified that the parent imidazole and 1-methylimidazole compounds had been subjected to both *in vitro* and *in vivo* testing as of the critical date, this corroborated by documentary evidence, and found to possess an inhibitory effect for thromboxane synthetase. Based upon this, Dr. Ramwell further testified that he would expect that *in vivo* testing of the imidazole derivatives of the phantom count would show that these compounds also possessed an inhibitory action for thromboxane synthetase, i.e., there would be a reasonable correlation [\*\*32] between *in vitro* test results and *in vivo* test results. This evidence was found sufficient by the Board as proof that the Japanese priority application had



disclosed a completed practical utility for the imidazole derivatives of the phantom count in inhibiting thromboxane synthetase in human or bovine platelet microsomes. *Cf. Rey-Bellet*, 493 F.2d at 1386-87, 181 U.S.P.Q. (BNA) at 457.

Cross argues that the *in vitro* utility disclosed by the Japanese priority application is not *per se* useful, and that more sophisticated *in vitro* tests, using intact cells, or *in vivo* tests are necessary to establish a practical utility.<sup>19</sup> Cross is arguing that there must be a rigorous correlation of pharmacological activity between the disclosed *in vitro* utility and an *in vivo* utility to establish a practical utility. We, however, find ourselves in agreement with the Board that, based upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative [\*\*33] evidence. *Cf. Nelson*, 626 F.2d at 856, 206 U.S.P.Q. (BNA) at 883-83.

19 Cross is seemingly arguing that the *in vitro* disclosure of the Japanese priority application is only a *potential* utility. See *Knapp v. Anderson*, 477 F.2d 588, 591, 177 U.S.P.Q. (BNA) 688, 691 (CCPA 1973).

Our predecessor court has accepted evidence of *in vivo* utility as sufficient to [\*1051] establish a practical utility. See, e.g., *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (CCPA 1980); *In re Jolles*, 628 F.2d 1322, 206 U.S.P.Q. (BNA) 885 (CCPA 1980); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 181 U.S.P.Q. (BNA) 453 (CCPA 1974).

Opinions of our predecessor court have recognized the fact that pharmacological testing of animals is a screening procedure for testing new drugs for practical utility. See, e.g., *In re Jolles*, 628 F.2d 1322, 1327, 206 U.S.P.Q. (BNA) 885, 890 (CCPA 1980). This *in vivo* testing is but an intermediate link in a screening chain which may eventually lead to [\*\*34] the use of the drug as a therapeutic agent in humans. We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vivo* utility. *Cf. Nelson*, 626 F.2d at 856, 206 U.S.P.Q. (BNA) at 883.

Today, under the circumstances of the instant case, where the Japanese priority application discloses an *in vitro* utility, i.e., the inhibition of thromboxane synthetase

in human or bovine platelet microsomes, and where the disclosed *in vitro* utility is supplemented by the similar *in vitro* and *in vivo* pharmacological activity of structurally similar compounds, i.e., the parent imidazole and 1-methylimidazole compounds, we agree with the Board that this *in vitro* utility is sufficient to comply with the practical utility requirement of § 101.

### 3. Enablement

[\*\*35] The Board found that the knowledge as to the use of the pharmacological activity disclosed in the Japanese priority application lay in the fact that the system was a microsome system, microsome systems admittedly being known to those skilled in the art. Employing a microsome assay, the skilled worker could determine the relative strength of the compounds of the count vis-a-vis the known parent imidazole and 1-methylimidazole compounds. Thus, the dosage in the microsome assay milieu could be determined without inventive skill or undue experimentation.

Since we have agreed with the Board that the practical utility for the imidazole derivatives of the phantom count lies in their pharmacological activity in the microsome environment, the how-to-use requirement of § 112 must be analyzed with reference to the microsome environment. We are confronted with a disclosure, similar to the situation before the court in *Bundy*, that fails to reveal dosages for the novel compounds *per se*. 642 F.2d at 434, 209 U.S.P.Q. (BNA) at 51. Although the Japanese priority application does disclose the fact that the imidazole derivatives of the phantom count possess a pharmacological activity [\*\*36] similar to the parent imidazole and 1-methylimidazole compounds, the priority application, unlike the application in *Bundy*, does not disclose dosages for the parent imidazole and 1-methylimidazole compounds.

We agree with the Board, however, that this deficiency in the Japanese priority application is not fatal. The testimonial evidence of Dr. Ramwell, corroborated by certain documentary evidence, showed that those skilled in the art had available, at the critical date, information as to approximate dosage levels for the parent imidazole and 1-methylimidazole compounds to produce an I[C50] effect, i.e., a 50% inhibition of thromboxane synthetase, in a microsome milieu. The objective of the pharmaceutical research undertaken by the parties was to discover imidazole derivatives having a potent inhibitory effect for thromboxane synthetase. Therefore, we believe it is logical, as did the Board, that the starting point for determining I[C50] dosage levels for the imidazole derivatives of the phantom count would be the I[C50] dosage levels of the parent imidazole and 1-methylimidazole compounds. The Board found that there was sufficient credible evidence that one skilled [\*\*37] in the art,

without the exercise of [\*1052] inventive skill or undue experimentation, could determine the I[C50] dosage level for the imidazole derivatives of the phantom count in the microsome environment. *Cf. Bundy, id.*, 209 U.S.P.Q. (BNA) at 51. We do not believe the Board erred in arriving at this conclusion. This is not a case such as *In re Gardner*, 57 C.C.P.A. 1207, 427 F.2d 786, 166 U.S.P.Q. (BNA) 138 (1970), where the CCPA held that the applicant's disclosure was nonenabling because inventive skill and undue experimentation would be required to discover appropriate dosages for humans, i.e., a therapeutic use. In the instant case, we are confronted with a pharmacological activity or practical utility, not a therapeutic use.

While we agree with the Board that the disclosure in the Japanese priority application is somewhat confusing with respect to the  $2.5 \times 10^{-8}$  level of molar concentrations, and that the 2-[p-(1-imidazolylmethyl)phenoxy]-acetic acid hydrochloride compound is outside the phantom count of the interference, this disclosed molar concentration, we believe, does provide some

probative value going towards the sufficiency of the Japanese priority [\*\*38] application for an enabling disclosure. The disclosed molar concentration would provide sufficient information as to an initial dosage level so that one skilled in the art could determine, without inventive skill or undue experimentation, the necessary molar concentrations for the imidazole derivatives of the phantom count to achieve the desired pharmacological effect, i.e., the 50% inhibition of thromboxane synthetase in human or bovine platelet microsomes.

The Board held the disclosure of the Japanese priority application adequate to satisfy the first paragraph of § 112. The burden is on Cross to show Board error in arriving at this conclusion, and we are not persuaded that Cross has successfully carried this burden. Accordingly, we are satisfied that the how-to-use requirement of § 112 has been complied with by the disclosures of the Japanese priority application.

AFFIRMED.